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human diabetes patient an effective amount of 1α-hydroxy vitamin D compounds such that diabetes symptoms are lessened.

Remarks

The Office Action has rejected all claims under 35 U.S.C. § 103. In light of the amendments above and arguments below, Applicants respectfully request reconsideration.

§ 103 Rejections

The Office Action has rejected claims 1 - 5 under 35 U.S.C. § 103 as being unpatentable over EURODIAB in view of Mathieu, et al., Mauricio, et al. and DeWille, et al.

The Examiner cites EURODIAB as teaching "a method of delaying the onset of diabetes in a human patient, comprising administering an effective amount of a vitamin D compound broadly . . . ." Applicants point out to the Examiner that the authors described ordinary vitamin D as possibly reducing the risk of developing Type I Diabetes. The present invention does not claim and, in fact, teaches away from the use of ordinary vitamin D to prevent diabetes. For example, Applicants note that NOD mice used in the examples of the specification have sufficient amounts of ordinary vitamin D in their diet. These animals developed diabetes quite clearly (as

disclosed in the specification and previous work in the field) so ordinary vitamin D cannot prevent diabetes.

Applicants have clarified claim 1 to be limited to 1α-hydroxy compounds and note that claims 2 and 3 specify activated vitamin D compounds or 1-hydroxylated forms of vitamin D.

Applicants note that Mathieu, et al., used in combination with EURODIAB, has a different mode of administration. Applicants were unable to confirm the success of the Mathieu, et al. mode of administration and have therefore only claimed oral administration. Applicants direct the Examiner to the specification, page 5, line 6 where Mathieu is distinguished from the present invention.

As for the Examiner's next citation, Applicants read Mauricio, et al. as discussing the role of 1,25 D_3 in diabetes and numerous other autoimmune diseases. A reading of Mauricio indicates that use of 1,25 D_3 may or may not be successful in diabetes treatment. It is certainly not possible to read Mauricio as teaching that 1,25 D_3 would necessarily be a successful diabetes treatment. Note the first paragraph in the right hand column on page 63, "However, this is still a matter of controversy since recent data on the effects of 1,25 D_3 on influence secretion *in vitro* showed no effect on glucose-

stimulated insulin secretion on rat islet . . . or even an inhibition by 1,25 D_3 on rat islet cultures and RIN cells. Although in the light of some of these studies the application of 1,25 D_3 as an enhancer of insulin secretion has been proposed in the field of diabetes mellitus, further research is warranted." (emphasis added)

In additionally addressing Mauricio, et al., Applicants enclose Exhibit A which contains additional disclosure regarding the vitamin D compound MC903, described in Mauricio as counteracting "the effective IL1β of accumulated insulin-releasing rat islets cultured for 48 hours in the presence of the cytokine." Exhibit A indicates that MC903 has an extremely short half life and lacks significant biological activity *in vivo*. Thus, MC903 would not be an appropriate therapeutic.

Applicants assert that one could not combine the Examiner's cited references to teach the success of the Applicants' cited compounds and mode of administration in delaying the onset of diabetes.

The Office Action next rejects claims 6 - 10 as unpantentable over Al-Qadreh, et al. in view of DeWille, et al. The Examiner cites Al-Qadreh as teaching administering 1α-hydroxyvitamin D_3 to human diabetes patients and notes that Al-Qadreh does not specifically

teach oral administration. DeWille is cited as incorporating vitamin D into a beverage, thereby teaching oral administration of vitamin D.

However, as Applicants have shown above, it is the oral administration of Applicants' compound that is important in diabetes treatment. DeWille does not teach oral administration to diabetes patients. Al-Qadreh does not teach any significance of administration mode and teaches away from oral administration. Additionally, Applicants questions whether Al-Qadreh, et al. teach amelioration of diabetes symptoms. Al-Qadreh, et al. is directed to the treatment of osteopenia in diabetic children and does not address treatment of diabetes itself.

A Petition and Fee for One Month Extension of Time is enclosed. No other fees are believed necessary to enter this response. However, if a fee is necessary please charge Deposit Account 17-0055.

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Group Art Unit:	1617
Examiner:	K. Stiller

Commissioner For Patents
Washington, D.C. 20231

MARKED UP VERSION OF THE CLAIMS

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1. (Amended) A method of delaying the onset of diabetes in a human patient, comprising the step of orally administering to the patient an effective amount of a 1α-hydroxy vitamin D compound such that the onset of diabetes or diabetes symptoms is slowed.

6. (Amended) A method of reducing the severity of diabetes symptoms comprising orally administering to a human diabetes patient an effective amount of 1α-hydroxy vitamin D compounds such that diabetes symptoms are lessened.